

**REMARKS****I. Status of the Claims**

Claim 1 is amended.

Claims 1-3, 17-19, 21 and 22 are pending.

The examiner did not enter the amendment December 19, 2006 alleging that the amendment raised “new issues.”

**II. Amended claims overcome rejections under 35 U.S.C. § 112**

Claim 1 is amended. Support for claim amendments can be found at least on page 3, line 1 (“related non-target proteins”) of the specification as filed. Support can also be found on page 3, lines 23-26 (“Amino acid sequences of at least 4 in length are selected from at least one of the protein sequences that showed some degree of homology to the target protein. Closest matches are preferred”), which implies “related” non-target proteins are useful for homology comparisons. In addition, illustrations shown on FIGS. 2a-b also imply that related human colonizing pathogens were compared in the context of non-target proteins. For example, *H. pylori* flagellar sheath adhesion protein was compared with *Streptococcus pneumoniae* pspA and *Mycoplasma hominis* Lp1 homologous sequences on FIGS. 2a-b. Given the guidance in the specification and one of the aims of the immunogenic target peptides—to avoid cross-reactivity with other related proteins, a person of ordinary skill in the art, would readily appreciate that related non-target proteins refer to either human proteins present in human tissues (when human proteins are compared) or proteins present in related colonizing human pathogens (disease pathogens). Therefore, immunogenic target peptides are compared not to every available sequence in the database, but only to sequences from related non-target proteins. This can be done either by restricting the range to include only a desired pathogen or a group of pathogens (“related”), or by simply ignoring those matches that identify sequences from unrelated sources.

On pages 2-3 of the action, the examiner mentions that step (d) of claim requires “comparative proteins”. However, on the Amendment and Response filed March 27, 2006, applicants, at the suggestion of the examiner and his supervisor, replaced “comparative proteins” with “non-target proteins” for clarity. The amendments filed on March 27, 2006 reflect those changes.

Claim 1 is further amended to relate what is in the specification. Peptides from related non-target proteins that are more than 50% homologous to candidate peptides from target proteins, do not remove the candidate peptide from use if the peptide from a related, non-target protein is not hydrophilic, that is, not present in the surface of the non-target proteins.

The intent clearly expressed is that the goal of comparing candidate peptides to related non-target protein is to avoid cross-reactivity leading to non-specific diagnosis. As stated in page 2, lines 25-28; page 3, lines 17-22, and in claim 1, one way to avoid cross-reactivity is to use a plurality of peptides in diagnosis, another is to show specific immunogenicity of the candidate peptide. Peptides from related non-targeted proteins will not stimulate immunogenic responses that interfere with diagnosis if they are not on the surface of their respective non-targeted proteins. Hydrophilic peptides are likely to be on the surface. Therefore, candidate peptides selected by algorithms of the present invention are confirmed as specific immunogens as shown in Example 1.

An example is illustrated herein. For example, a desired *H. pylori* adhesion protein HpaA sequence ("target protein") is obtained from the GenBank using the gene identifier gi19338964 or accession number AAL86898.1. The sequence is

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1 mktnghfkdf awkkcllgas vvallvgcsp hiietneval klnyhpasek vqaldekill
61 lrpafqysdn iakeyenkfk nqtalkveqi lqnqgykvin vdssdkddfs faqkkegyla
121 vamngeivlrpdpkrtdqkksepallfstgldkmegvlipagfikvtile pmsgesldsf
181 tmdlseldiq ekflktthss hsgglvstmv kgtdnsndai ksalnkifan imqeiddklt
241 qknlesyqkd akelknkrnr

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Then, a rolling sum hydrophilicity analysis is performed to identify one or more peptide structure (target peptide) that is present on the surface of the target protein. One such target peptide is MQEIDKK.

A BLAST analysis for short, nearly exact matches is performed with the MQEIDKK sequence. It can be found that none of the proteins from related normally human colonizing pathogens match this peptide and satisfy the elements of claim 1. Even if some external, pathogenic and non-pathogenic environment microorganismal proteins partially match, these are not as antigenically significant as *Helicobacter pylori* flagellar sheath adhesion HpaA protein (the principal target protein).

#### *H. pylori*

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Query 1      MQEIDKK 7
      MQEIDKK
Sbjct 232    MQEIDKK 238

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#### *Trichodesmium erythraeum*

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Query 1      MQEIDKK 7
      MQE+DKK
Sbjct 400    MQELDKK 406

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Even if some related non-target proteins have matching stretches to the target peptide, if those stretches are not antigenically significant (e.g., not present in the surface as determined by hydrophilicity), then the target peptides are not likely to elicit cross-reactivity, *i.e.*, have antigenic profiles that elicit an immune response specific for the target protein. In addition, putative or

hypothetical proteins merely from annotated sequences of unrelated microorganisms are not considered.

The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984).

A specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 57 C.C.P.A. 946, 950 (C.C.P.A. 1970).

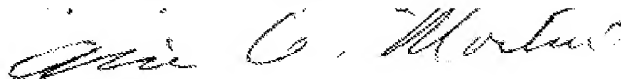
An applicant need not have actually reduced the invention to practice prior to filing. The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it. *In Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987).

### **III. Conclusion and Summary**

In view of the arguments presented herein, please allow all pending claims. Applicant requests an interview if there are remaining issues.

No other fees are believed due at this time, however, please charge any additional deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21417/92378).

Respectfully submitted,



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